Rejections Under 35 U.S.C. § 112, second paragraph

The Examiner has rejected claim 5 as being indefinite for the recitation of the phrase "fine specificity." Applicants have amended claim 5, deleting the term "fine." Amended claim 5 now indicates that the anitbodies have the same specificity of binding as the antibody of claim 4. It is understood in the art that any antibodies competing for binding to a specific antigen are defined to have the same specificity.

Although the Examiner has also issued a rejection for claim 6, there is no indication as to what in particular is found to be indefinite. Applicants therefore respectfully request an explanation as to the specific reason for this rejection.

Rejections Under 35 U.S.C 112, first paragraph

The Examiner has rejected claim 6 for lack of enablement. The Examiner acknowledges that the Specification is enabling for a single epitope recognized by mAB HE2, but contends that the Specification does not reasonably provide enablement for antibodies directed to different epitopes. Applicants respectfully traverse.

Applicants first note that claim 6 has been amended to clearly indicate that two or more antibodies that are directed against different membrane antigens or against different epitopes of a membrane antigen are used in combination with each other. Examples of tumor-associated membrane antigens are provided in the

Specification on page 4, lines 13-21. Thus, in view of the amendment to claim 6 and the disclosure in the instant Specification, the Examiner's comments that it would require a great deal of experimentation to determine which membrane-associated antibodies are useful and are able to react to the membrane antigen is simply wrong.

The Examiner also indicates that the working examples using a single antibody (mAB HE2) is not sufficient to support the breath of the claims where the scope encompasses multiple antibodies with different epitope reactivity. Applicants enclose the Declaration of Dr. Hans Loibner. Here, Dr. Loibner presents supplemental experimental results to support enablement. Specifically, he shows that goats immunized with two different antibody preparations (HE2 antibody and 73-3 antibody) induced antibodies against the EpCam molecule. The HE2 and the 73-3 antibodies bind different epitopes of the EpCam molecule. Dr. Loibner also presents results from Rhesus monkeys that were immunized with HE2 and KS1/4 antibodies. Again, specific antibodies were isolated from the immune sera of both groups. That is, vaccination with both anti-EpCAM antibodies induced an antibody titer specific for EpCAM positive tumor cells. Applicants submit that these experimental results presented in Dr. Loibner's Declaration provide sufficient support for enablement of the scope of the instant claims. In view of this, Applicants respectfully request reconsideration and removal of the rejection.

The Examiner has rejected claims 1-9 for lack of enablement, contending that the instant Specification has insufficient disclosure to support enablement for use of the composition as a prophylactic compound for the prevention of cancer. The Examiner further contends that the quantity of experimentation required to prevent cancer is high because it has been shown that a cancer vaccine can only, at best, be used as therapeutic and not as a prophylactic. Applicants respectfully traverse.

Applicants have amended claim 1 to clearly indicate that the composition can be used to prevent the development of metastasis. Applicants note that although the prior art teaches that vaccines against cancer are difficult, recent clinical trial results indicate that vaccination with pharmaceutical compositions according to the invention decreases circulating tumor cells in cancer patients (see Proceedings of ASCO, Vol. 21, 2002, Abstracts 1898 and 1899, enclosed). A decrease in circulating tumor cells is indicative of suppression of metastasis formation. This effect is obtained by prophylactic vaccination of cancer patients to suppress metastasis formation. Thus, Applicants submit that this supplemental objective evidence supports the enablement of claim 1-9 and therefor request reconsideration and removal of the rejection.

Rejections Under U.S.C. § 102

The Examiner has rejected claims 1-3 under U.S.C. § 102(a) as being anticipated by Braun et al. (Clinical Cancer Research, December 1999, 5:399-4004). Braun et al. discloses a monoclonal antibody developed in a mouse that is specific for EpCam and further discloses the use of this antibody for the elimination of tumors in patients by intravenous infusion of 500 mg of the antibody. Applicants respectfully traverse.

The instant application claims priority to Swiss Application No. 1999 0051/99, filed January 13, 1999. Applicants have enclosed a certified English translation of this priority document. As a consequence, the Braun reference, dated December 1999 cannot be used to support a rejection based on novelty or obviousness. Thus, Applicants respectfully request that the novelty rejection be removed.

NO Translation Present

Rejections Under U.S.C. § 103

The Examiner has rejected claim 7 for obviousness, citing Braun et al. (1999) in view of Pardoll (1993). The Examiner contends that while Braun et al. does not specifically disclose administration of an adjuvant in combination with an antibody to administer the compound, Pardoll cures this deficiency by teaching the use of adjuvants in combination with vaccines for the treatment of cancer. The Examiner further contends that it would have been

obvious to one of ordinary skill in the art to develop a compound for treating cancer comprising an antibody against EpCam and an adjuvant because the prior art provides sufficient motivation to practice the invention as claimed. Here, the Examiner bases his contention on the fact that Braun et al. teaches the use of EpCam as a form of treatment in cancer. Applicants respectfully traverse.

As noted above, Braun cannot be used as a reference to support an obviousness rejection because it was published after the priority date of the instant application. While Pardoll does teach using adjuvants in combination with vaccines for cancer treatment, there is no cellular membrane antigen, let alone EpCam, or antibodies directed against these antigens listed among the suitable tumor-specific antigens in Table 1. Thus, there is no suggestion for a skilled artisan to prepare an immunogenic anti-EpCam antibody preparation in view of Pardoll alone. In view of this, Applicants request reconsideration and removal of the rejection.

In view of the above remarks, all of the claims remaining in the case, including amended and newly submitted claims, are submitted as defining non-obvious, patentable subject matter.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact Leonard R. Svensson (Reg. No. 30,330) in Costa

Mesa, CA at 714-708-8555, to conduct an interview in an effort to expedite prosecution in connection with the present application.

Attached hereto is a marked-up version of the changes made to the application by this Amendment.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. §§ 1.16 or 1.17; particularly, extension of time fees.

Respectfully submitted,

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LRS/SWG/sbp
0147-0229P

Attachment: Version with Markings to Show Changes Made

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail with postage prepaid, in an envelope addressed to: Commissioner of Patents and Trademarks, Washington, D.C. 20231 on: Aug 8, 2002
(Date of Deposit)

BIRCH, STEWART, KOLASCH & BIRCH, LLP

Aug 8, 2002

VERSION WITH MARKINGS TO SHOW CHANGES MADE

IN THE CLAIMS:

The claims have been amended as follows:

1. (Twice Amended) A pharmaceutical composition for vaccination [against cancer] to actively immunize cancer patients for the prevention of the development of metastasis and treatment of cancer disease comprising at least one antibody directed against the cellular membrane antigen EpCAM.

5. (Twice Amended) The pharmaceutical composition of any one of claims 1-3, wherein said antibody has the same [fine] specificity of binding as that antibody defined in claim 4.

6. (Twice Amended) The pharmaceutical composition of claim 1, wherein [said antibodies are directed against different epitopes of the membrane antigen] two or more antibodies, which are directed against different membrane antigens or against different epitopes of a membrane antigen, are used in combination with each other.